

**FIG. 1**

cons.aa	G	G	G	V	A	K	E
hTGfBR-II	L	D	T	V	G	K	R
mActR-IIB	F	A	E	V	V	K	A
mActR-II	K	Q	N	T	S	E	Q
<i>daf-1</i>	F	E	T	V	A	V	K
subdomains	I	II	III	IV			

hTGFR-II  
mActR-IIb  
mActR-II  
*daf-1*  
subdomains

cons.aa	DLK	N	DFG
hTGfBR-II	-GRPKMPIVHRDLKSSN	ILVKNDLTCC	LCDFGLSLRL---
mActR-IIB	GECHKPSIAHRDFKSK	NVLLKSDLTAV	LADFGLAVRF---
mActR-II	-DGHKPAISHRDIKSK	NVLLKNNLTAC	IADFGLALKF---
daf-1	-ESNKPAMAHARDIKSK	NIMYKNDLTCA	IGDLGLSLSKPEDA
subdomains	VI-B	VII	VIII



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## FIG. 2A

a.a            C   C   E   G   N   M   C  
5' GCGGATCCTGTTGTGAAGGNAATATGTG 3'  
      BAMHI   C   C   G        C

## FIG. 2B

a.a            V    A   V   K   I   F  
5' GCGGATCCGTCGCAGTCAAAATTTT 3'  
      BamHI        G   C   G   G   C  
                  T   T   T        A

## FIG. 2C

a.a            R   D   I   K   S   K   N  
5' GCGGATCCGCGATATTTAAAGCAA 3'  
      BAMHI        A   C   C   GTCT  
                  G        A

## FIG. 2D

a.a            E   P   A   M   Y  
5' CGGAATTCTGGTGCCATATA  
      EcoRI   G   G        G  
              A   A

FIG. 3A

MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNNDMIVTDNNGAV	ActR-II
MTAPWAA	ActR-IIB
MEAAVAAAPRRRL	TBR-II
MTLGSPRKGLLMLLMALV	TBR-I/ALK-5
MVDGVMILPVL	ALK-1
MLLRSSGKLN	ALK-2
MLLRSSGKLN	ALK-3
MLLRSSGKLN	ALK-4
MLLRSSGKLN	ALK-6
MTQLYIYIRLLGAYLFIISRVQGQNLD	ActR-II
MTQLYIYIRLLGAYLFIISRVQGQNLD	ActR-IIB
MTQLYIYIRLLGAYLFIISRVQGQNLD	TBR-II
MTQLYIYIRLLGAYLFIISRVQGQNLD	TBR-I/ALK-5
MTQLYIYIRLLGAYLFIISRVQGQNLD	ALK-1
MTQLYIYIRLLGAYLFIISRVQGQNLD	ALK-2
MTQLYIYIRLLGAYLFIISRVQGQNLD	ALK-3
MTQLYIYIRLLGAYLFIISRVQGQNLD	ALK-4
MTQLYIYIRLLGAYLFIISRVQGQNLD	ALK-6
SETQECLEFFNANWELER	ActR-II
SETQECLEFFNANWELER	ActR-IIB
SETQECLEFFNANWELER	TBR-II
SETQECLEFFNANWELER	TBR-I/ALK-5
SETQECLEFFNANWELER	ALK-1
SETQECLEFFNANWELER	ALK-2
SETQECLEFFNANWELER	ALK-3
SETQECLEFFNANWELER	ALK-4
SETQECLEFFNANWELER	ALK-6
ISGSIIEIVKQGC	ActR-II
ISGSIIEIVKQGC	ActR-IIB
ISGSIIEIVKQGC	TBR-II
ISGSIIEIVKQGC	TBR-I/ALK-5
ISGSIIEIVKQGC	ALK-1
ISGSIIEIVKQGC	ALK-2
ISGSIIEIVKQGC	ALK-3
ISGSIIEIVKQGC	ALK-4
ISGSIIEIVKQGC	ALK-6

[illegible]

-	-	-	-	-	-	P	T	Q	D	P	G	P	P	P	S	-	-	P	L	L	G	L	-	-	-	K	P	L	Q	L	E	V	K	A	R	G	R	ActR-II							
D	G	C	A	D	S	F	K	P	L	P	F	Q	D	P	G	P	P	P	S	-	-	P	L	V	G	L	-	-	K	P	L	Q	L	E	I	K	A	R	G	R	ActR-IIB				
E	H	C	A	I	L	E	D	D	R	S	D	I	S	S	T	C	A	N	I	N	H	N	T	E	L	-	-	L	P	I	E	L	D	T	L	V	G	K	G	R	TβR-II				
-	-	-	G	T	T	L	K	D	L	I	Y	D	M	T	T	S	G	S	G	S	G	L	P	L	V	Q	R	T	I	A	R	T	I	V	L	Q	E	S	I	G	K	G	R	TβR-I/ALK-5	
E	Q	G	D	T	M	L	G	D	L	L	D	S	D	C	T	T	G	S	G	S	G	L	P	F	L	V	Q	R	T	V	A	R	Q	V	A	L	V	E	C	V	G	K	G	R	ALK-1
N	V	G	D	S	T	L	A	D	L	L	D	H	S	C	T	S	G	S	G	S	G	L	P	F	L	V	Q	R	T	V	A	R	Q	I	T	L	E	C	V	G	K	G	R	ALK-2	
-	-	-	G	E	S	L	K	D	L	I	D	Q	S	Q	S	S	G	S	G	S	G	L	P	L	V	Q	R	T	I	A	K	Q	I	Q	M	V	R	Q	V	G	K	G	R	ALK-3	
-	-	-	D	K	T	L	Q	D	L	V	Y	D	L	S	T	S	G	S	G	S	G	L	P	L	F	V	Q	R	T	V	A	R	T	I	V	L	Q	E	I	I	G	K	G	R	ALK-4
-	-	-	G	E	S	L	R	D	L	I	E	Q	S	Q	S	S	G	S	G	S	G	L	P	L	V	Q	R	T	I	A	K	Q	I	Q	M	V	K	O	I	G	K	G	R	ALK-6	

FIG. 3C

FGCVWKAQLLN	---	---	---	---	EYVAVKIF	PIQDKQ	SWQNKQ	YEVY	YEVY	SLPGM	ActR-II
FGCVWKAQLMN	---	---	---	---	DFVAVKIF	PLQDKQ	SWQNKQ	YEVY	YEVY	SLPGM	ActR-IIB
FAEYVWKAQ	---	---	---	---	FFVAVKIF	PPYEE	YASWKT	YEVY	YEVY	SLPGM	TBR-II
FGVWVWKGK	---	---	---	---	FFVAVKIF	SSSRDE	QSWFRRE	YEVY	YEVY	SLPGM	TBR-I/ALK-5
YGEVWVWKG	---	---	---	---	FFVAVKIF	SSSRDE	QSWFRRE	YEVY	YEVY	SLPGM	ALK-1
YGEVWVWKG	---	---	---	---	FFVAVKIF	SSSRDE	QSWFRRE	YEVY	YEVY	SLPGM	ALK-2
YGEVWVWKG	---	---	---	---	FFVAVKIF	SSSRDE	QSWFRRE	YEVY	YEVY	SLPGM	ALK-3
YGEVWVWKG	---	---	---	---	FFVAVKIF	SSSRDE	QSWFRRE	YEVY	YEVY	SLPGM	ALK-4
YGEVWVWKG	---	---	---	---	FFVAVKIF	SSSRDE	QSWFRRE	YEVY	YEVY	SLPGM	ALK-6

II

KHENILQFI	GA	EKR	GT	SV	DV	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	W	ActR-II
KHENILQFI	GA	EKR	GT	SV	DV	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	W	ActR-IIB
KHENILQFI	GA	EKR	GT	SV	DV	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	W	TBR-II
RHENILGFI	AS	DM	TS	RN	SS	Q	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	TBR-I/ALK-5
RHENILGFI	AS	DM	TS	RN	SS	Q	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	ALK-1
RHENILGFI	AS	DM	TS	RN	SS	Q	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	ALK-2
RHENILGFI	AS	DM	TS	RN	SS	Q	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	ALK-3
RHENILGFI	AS	DM	TS	RN	SS	Q	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	ALK-4
RHENILGFI	AS	DM	TS	RN	SS	Q	LWL	IT	AF	HE	KG	SL	DE	KL	AN	VVS	ALK-6

V

NE LCHIAETM	AR	GL	AY	LH	ED	IP	-	GL	KD	GH	KP	AI	SH	RD	IK	SK	NV	LL	ActR-II
NE LCHVVAET	MS	RG	LS	YL	HE	VP	WC	RG	EG	HK	PP	SI	AH	RD	FK	SK	NV	LL	ActR-IIB
ED LRLGSS	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	TBR-II
EGMIKLA	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	TBR-I/ALK-5
H LALRLAV	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	ALK-1
V SCLRIIVL	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	ALK-2
RALLKLA	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	ALK-3
EGMIKLA	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	ALK-4
K SMLKLA	SL	AR	GL	AY	LH	SD	HT	PC	-	GR	PP	MI	VH	RD	LK	SK	NV	LL	ALK-6

VIB

VIA

FIG. 3D

K	N	N	L	T	A	C	I	A	D	F	G	L	A	V	R	L	K	F	E	A	G	K	S	A	G	D	-	-	T	H	G	Q	V	G	T	R	R	Y	M	A	P	E	V	L	E	G	ActR-II
K	S	D	L	T	A	V	L	A	D	F	G	L	A	V	R	L	K	F	E	P	G	K	P	P	G	D	-	-	T	H	G	Q	V	G	T	R	R	Y	M	A	P	E	V	L	E	G	ActR-IIB
K	N	D	L	T	C	C	L	C	D	F	G	L	S	L	R	L	D	P	T	L	S	V	D	D	L	A	N	S	G	Q	V	G	T	A	R	Y	M	A	P	E	V	L	E	S	TβR-II		
K	K	N	G	T	C	C	I	A	D	L	G	L	A	V	R	H	D	S	A	T	D	T	I	D	I	A	P	N	H	R	V	G	T	K	R	Y	M	A	P	E	V	L	D	TβR-I/ALK-5			
K	S	N	L	Q	C	C	I	A	D	L	G	L	A	V	M	H	S	Q	S	D	Y	L	D	I	G	N	N	P	R	V	G	T	K	R	Y	M	A	P	E	V	L	D	E	ALK-1			
K	K	N	G	Q	C	C	I	A	D	L	G	L	A	V	M	H	S	Q	S	T	N	Q	L	D	V	G	N	P	R	V	G	T	K	R	Y	M	A	P	E	V	L	D	E	ALK-2			
K	K	N	G	S	C	C	I	A	D	L	G	L	A	V	K	F	N	S	D	T	N	E	V	D	V	P	L	N	T	R	V	G	T	K	R	Y	M	A	P	E	V	L	D	E	ALK-3		
K	K	N	G	M	C	I	A	D	L	G	L	A	V	R	H	D	A	V	T	D	T	I	D	I	A	P	N	Q	R	V	G	T	K	R	Y	M	A	P	E	V	L	D	E	ALK-4			
K	K	N	G	T	C	C	I	A	D	L	G	L	A	V	K	F	I	S	D	T	N	E	V	D	I	P	P	N	T	R	V	G	T	K	R	Y	M	P	E	V	L	D	E	ALK-6			

VII

VIII

A	I	N	F	Q	R	-	D	A	F	L	R	I	D	M	Y	A	M	G	L	V	L	W	E	L	A	S	R	C	T	A	A	D	G	P	V	D	E	Y	M	L	P	F	E	E	ActR-II	
A	I	N	F	Q	R	-	D	A	F	L	R	I	D	M	Y	A	M	G	L	V	L	W	E	L	V	S	R	C	K	A	A	D	G	P	V	D	E	Y	M	L	P	F	E	E	ActR-IIB	
R	M	N	L	E	N	A	E	S	F	K	Q	T	D	V	Y	S	M	A	L	V	L	W	E	M	T	S	R	C	N	A	V	-	G	E	V	K	D	Y	E	P	P	F	E	G	S	TßR-II
S	I	N	M	K	H	F	E	S	F	K	R	A	D	I	Y	A	M	G	L	V	F	E	I	A	R	R	C	S	I	-	G	G	I	H	E	D	Y	Q	L	P	Y	D	TßR-I/ALK-5			
Q	I	R	T	D	C	F	E	S	Y	K	W	T	D	I	W	A	F	G	L	V	L	W	E	I	A	R	R	T	I	V	-	N	G	I	V	E	D	Y	R	P	P	F	Y	D	ALK-1	
T	I	Q	V	D	C	F	D	S	Y	K	R	V	D	I	W	A	F	G	L	V	L	W	E	V	A	R	R	M	V	S	-	N	G	I	V	E	D	Y	K	P	P	F	Y	D	ALK-2	
S	L	N	K	N	H	F	Q	P	Y	I	M	A	D	I	Y	S	F	G	L	I	I	W	E	M	A	R	R	C	I	T	-	G	G	I	V	E	E	Y	Q	L	P	Y	N	ALK-3		
T	I	N	M	K	H	F	D	S	F	K	C	A	D	I	Y	A	L	G	L	V	Y	W	E	I	A	R	R	C	N	S	-	G	G	V	H	E	E	Y	Q	L	P	Y	D	ALK-4		
S	L	N	R	N	H	F	Q	S	Y	I	M	A	D	M	Y	S	F	G	L	I	L	W	E	I	A	R	R	C	V	S	-	G	G	I	V	E	E	Y	Q	L	P	Y	H	D	ALK-6	

IX

X

E	I	G	Q	H	P	S	L	E	D	M	Q	E	V	V	V	H	K	K	K	R	P	V	L	R	D	Y	W	Q	K	H	A	G	M	A	M	L	C	E	T	I	E	E	C	W	ActR-II	
E	I	G	Q	H	P	S	L	E	E	L	Q	E	V	V	V	H	K	K	K	M	R	P	T	I	K	D	H	W	L	K	H	P	G	L	A	Q	L	C	V	T	I	E	E	C	W	ActR-IIB
K	V	R	E	H	P	C	V	E	S	M	K	N	V	L	R	D	R	G	R	P	P	I	P	S	F	W	L	N	H	Q	G	I	Q	M	V	C	E	T	L	T	E	C	W	TβR-II		
L	V	P	S	D	P	S	V	E	E	M	R	K	V	V	C	E	Q	K	L	R	P	P	I	P	N	R	W	Q	S	C	E	A	L	R	V	M	A	K	I	M	R	E	C	W	TβR-I/ALK-5	
V	V	P	N	D	P	S	F	E	D	M	K	K	V	V	C	V	D	Q	Q	T	P	P	I	P	N	R	L	A	A	D	P	V	L	S	G	L	A	Q	M	M	R	E	C	W	ALK-1	
V	V	P	N	D	P	S	F	E	D	M	R	K	V	V	C	V	D	Q	Q	R	P	P	I	P	N	R	W	F	S	D	P	T	L	T	S	L	A	K	L	M	K	E	C	W	ALK-2	
M	V	P	S	D	P	S	Y	E	D	M	R	E	V	V	C	V	K	R	L	R	P	P	I	V	S	N	R	W	N	S	D	E	C	L	R	A	V	L	K	L	M	S	E	C	W	ALK-3
L	V	P	S	D	P	S	I	E	E	M	R	K	V	V	C	D	Q	K	L	R	P	P	I	P	N	W	Q	S	Y	E	A	L	R	V	M	G	K	M	M	R	E	C	W	ALK-4		
L	V	P	S	D	P	S	Y	E	D	M	R	E	I	V	C	M	K	K	L	R	P	P	S	F	P	N	R	W	S	S	D	E	C	L	R	Q	M	G	K	L	M	T	E	C	W	ALK-6

FIG. 3E

DHDAE[ARL]SAGCVGERITQMRLTNIITTEDIVTVVVTMVTNVDFP ActR-II  
 DHDAE[ARL]SAGCVEERV[SLIR]RVNGTTSDCLVSLVTSTNVDDL ActR-IIB  
 DHDP[EARL]TAQCVAERFSELEHLDRLSGRSCSEKIPEDGSLNTT TBR-II  
 YAN[GAARL]TALRIKKTL[SLSQ]QEGIKM(503) TBR-I/ALK-5  
 YPNP[SAARL]TALRIKKTL[QKIS]NSPEKPKVIQ(503) ALK-1  
 YQNP[SAARL]TALRIKKTL[TKID]NSL[DKL]KTDC(509) ALK-2  
 AHNPA[SR]LTALRIKKTL[AKM]VESQDVKI(532) ALK-3  
 YAN[GAARL]TALRIKKTL[SLSV]QEDVKI(505) ALK-4  
 AQNPA[SR]LTALRIKKTL[AKM]SE[SLQ]DIKL(502) ALK-6

XI

PKESSL (513) ActR-II  
 PKESSI (536) ActR-IIB  
 K (567) TBR-II

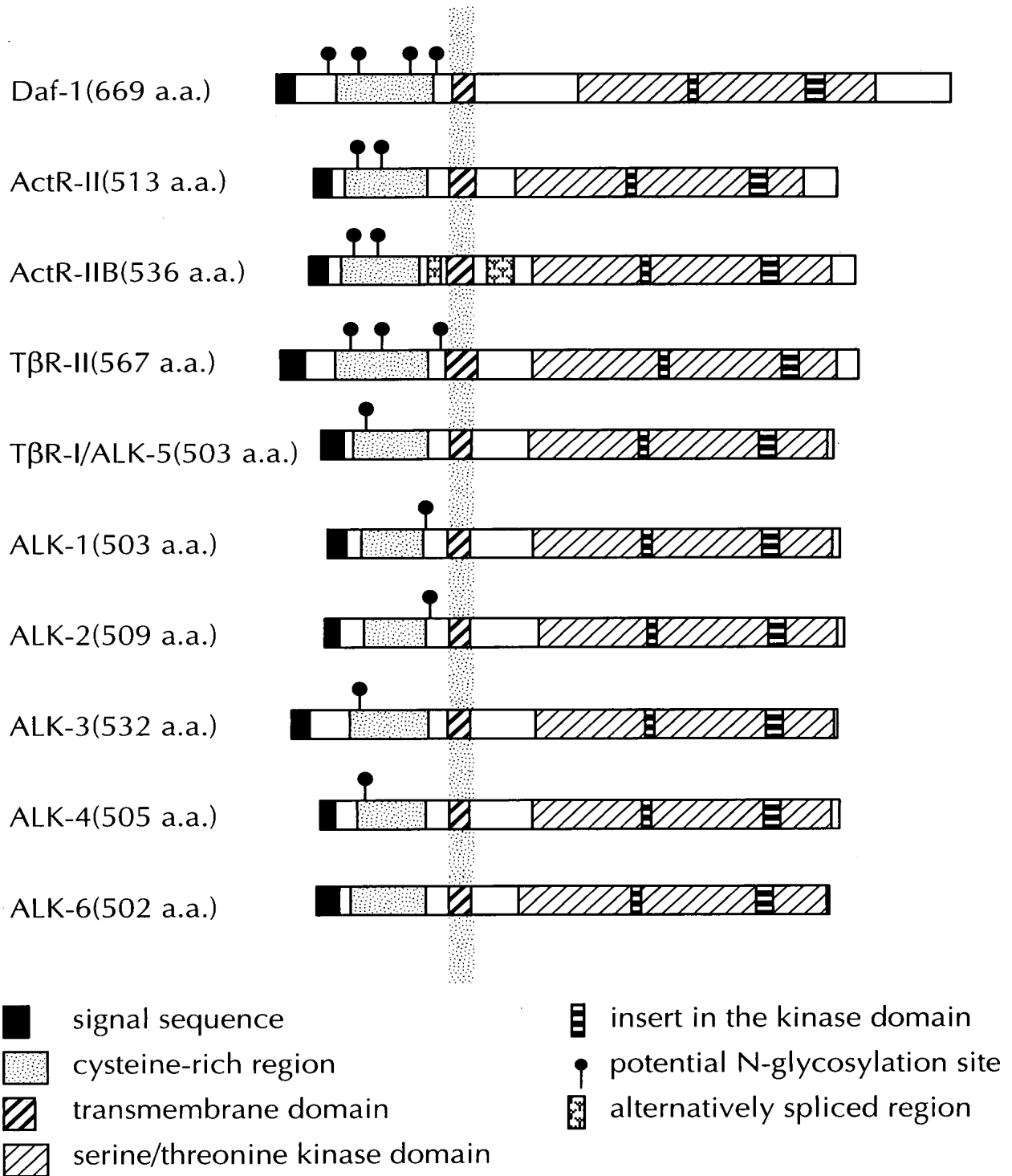


FIG. 4



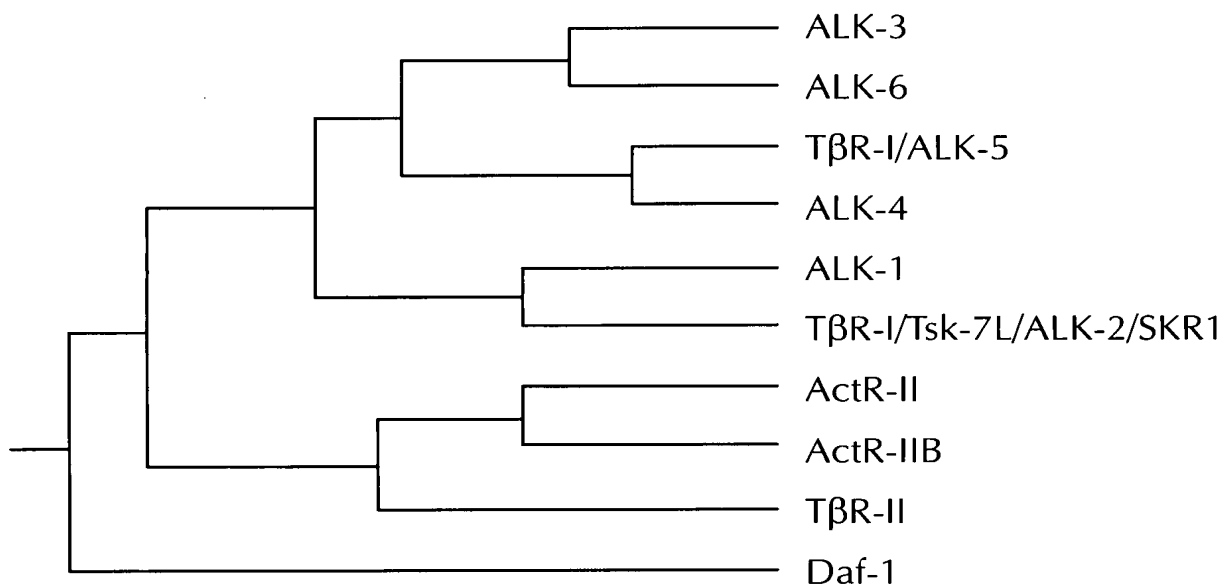
**FIG. 5**

[illegible][illegible]

**FIG. 6**

ALK-2	ALK-3	ALK-4	ALK-5	ActR-II	ActR-IIB	TβR-II	daf-1	
79	60	61	63	40	40	37	39	ALK-1
	63	64	65	41	39	37	39	ALK-2
		63	65	41	38	37	39	ALK-3
			90	41	40	39	42	ALK-4
				42	40	41	43	ALK-5
					78	48	35	ActR-II
						47	32	ActR-IIB
							34	TβR-II

**FIG. 7**





**FIG. 8**

FLAG-Smad5	-	+	+	+
c.a. ALK1-HA	-	-	+	-
c.a. ALK5-HA	-	-	-	+

IP : anti-FLAG  
Blot : anti-phosphoserine



IP : anti-FLAG  
Blot : anti-FLAG



IP : (-)  
Blot : anti-HA

